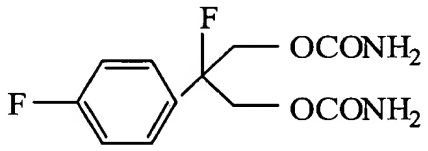
Remarks

On October 16, 2001, in response to a telephonic Restriction Requirement, applicants provisionally elected the invention of Group I, claims (in part) 4, 5, 6-8, 9-17. Applicants hereby affirm that election, and designate the compound



as the single elected species. Claims 1-3 have been canceled and claims 6-17 have been amended to remove the non-elected subject matter. New claims 18-29 have been added to claim further embodiments of the elected subject matter. Support for the new claims is found throughout the specification, and more particularly, for claim 18, on page 7, compound **13** and page 9, compound **24**; for claim 19, on page 3, lines 8-24; claims 20-26 on pages on page 11, line 2 through page 12, line 11 and page 13, lines12-22; and claims 27-29 on page 1, lines 11-12. These amendments are not made for reasons relating to patentability, but rather to advance the prosecution of the application. All pending claims, as amended herein, are believed to read on the elected species.

The Examiner has indicated that the Information Disclosure Statements submitted by applicants on 12/14/01 (mailed 11/20/01), 1/10/02 (mailed 12/17/02), 1/28/02 (mailed 12/19/02) and 2/4/02 (mailed 1/15/02) failed to include a legible copy of each cited reference. The undersigned attorney hereby states that copies of the cited references were provided with each of the submitted Invention Disclosure Statements. However, to assist the Examiner's review of this application, applicants have enclosed copies of each of the previously submitted Invention Disclosure Statements with copies of each of the cited references. Applicants also submit a copy of our post card receipts with the date stamp of the USPTO indicating the receipt of the original Invention Disclosure Statements and prior art references. However, the return post card for the first submitted Invention Disclosure Statement (mailed on November 20, 2001) has not been received by applicant and therefore is not included.

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Applicants respectfully submit that the previously submitted Invention Disclosure Statements fully complied with 37 CFR 1.98(a)(2) and therefore no fees are believed to be due for the resubmission of these Invention Disclosure Statements. If this belief is in error, the Commissioner is hereby authorized to charge any fees due for this submission to Deposit Account No. 50-0423.

Correction of Inventorship

The Examiner has correctly noted that the present application claims priority to previous applications that name a different inventive entity. The present application (US Serial No: 09/925,224) is a straight continuation of International Application No: PCT/US00/03147 (which claims priority to US Provisional Applications 60/119,254, 60/136,881 and 60/137,204). The invention described in International Application No: PCT/US00/03147 is the invention of the inventors named in the present US continuation application, and thus the parent international application does not constitute prior art for US Serial No: 09/925,224.

During the prosecution of the parent international application, in anticipation of filing a US national stage application, the undersigned attorney conducted a review of inventorship for the claimed subject matter. This review revealed that an individual (Christine Dieckhaus) who was not named on the international application believed herself to be an inventor of some of the claimed subject matter. Further investigation confirmed that Christine Dieckhaus should have been named as an inventor on the international application. This conclusion was made near the time when national stage applications were due to be filed. Accordingly, upon filing the present US continuation application a Declaration was prepared naming Tim MacDonald, Thomas Miller, Chuck Thompson and Christine Dieckhaus as co-inventors.

The undersigned attorney believed that since an executed Oath or Declaration had not been previously executed for this application, and since applicants were claiming priority under 35 USC § 120 that the filing of the executed combined Oath and Declaration cured the defect in inventorship. However, to expedite the prosecution of this application, applicants submit

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herewith a Request under 37 CFR § 148(a) to correct the inventorship and add Christine Dieckhaus as a named co-inventor.

The application as filed correctly named Tim MacDonald, Thomas Miller, Chuck Thompson and Christine Dieckhaus as co-inventors. However, due to the cancellation of the non-elected subject matter, two of the originally named co-inventors are no longer inventors of at least one claim remaining in the application. Therefore applicants also submit with this Response a Request under 37 CFR § 148(b) to correct the inventorship of the application and delete Thomas Miller, Chuck Thompson from the list of named inventors. The claimed invention as amended herein is the invention of only Christine Dieckhaus and Tim MacDonald.

Double Patenting

Claims 1-17 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of US Patent Application Nos. 09/913,075 and 10/023,059. US application 09/913,075 will become abandoned in July of 2002, thus making the rejection over that application moot. Applicants note that the Examiner indicated he has not reviewed the claims of US Patent Application Nos. 09/913,075 and 10/023,059 because they were not yet available to him. To assist the Examiner's review of this matter, applicants submit herewith a copy of the pending claims in US application 10/023,059. If after reviewing the claims of US Application No. 10/023,059 the Examiner still asserts the obviousness-type double patenting rejection, applicants will submit any terminal disclaimers necessary to remove such a rejection.

Rejections under 35 USC § 112

Claims 4, 5, 6 and their dependencies have been rejected under 35 USC § 112, second paragraph as being indefinite with regard to the inclusion of proviso language in the claims. Applicants respectfully submit that there is nothing indefinite regarding the inclusion of the proviso language in the claims. However, applicants note that the proviso language was not

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placed in the claims to avoid some know prior art reference, and therefore, to expedite the prosecution of this matter applicants have amended the claims to remove the proviso language. This amendment is made to expedite the prosecution of the application.

Claim 6 is rejected under 35 USC § 112, second paragraph as being indefinite with regard to the term "neurological disorder." Applicants respectfully submit that the term is used in accordance with its standard meaning and includes any disease or abnormality that has a neurological basis. This includes neurologic diseases such as multiple sclerosis, Parkinson's disease, as well as diseases/disorders that are associated with seizures. Although the term may encompass numerous disease states, one of ordinary skill would readily appreciate whether or not a diseases/disorders relates to neurology. For example, as noted on page 4, line 11-14 and now claimed in claims 25-27, the felbamate derivative of the present invention can be used to significantly reduce the incidence and severity of epileptic seizures. Applicants respectfully submit that one would appreciate whether or not their acts fall within the scope of the claims, and thus the language complies with 35 USC § 112, second paragraph.

Claim 9 stands rejected under 35 USC § 112, second paragraph as being indefinite with regard to the phrase "tissue damage resulting from localized hypoxic conditions." Applicants respectfully submit that the present compounds have neuropotective activities that prevent tissues from being damaged from conditions that cause localized low oxygen levels. The protective effect is believed to be unrelated to the cause of the low oxygen level, and thus any condition or disorder that causes low oxygen levels should be treatable with the compounds of the present invention. As applicants noted on page 2, lines 3-8 of the specification:

> Felbamate has also been reported to have efficacy in reducing cellular damage resulting from vascular reperfusion (US Patent No. 5,462,966) and preventing and treating tissue damage resulting from an ischemic event (US Patent No. 5,055,489). For example, compositions comprising felbamate can be administered to control or prevent hypoxic damage resulting from stroke and other cerebral ischemic events.

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Applicants have shown that the present derivatives have similar properties to the parent felbamate compound, and thus the derivatives are anticipated to display the same broad neuroprotective activities as have been demonstrated for the parent compound. Therefore, applicants have claimed the use of the derivative compounds for limiting the tissue/cellular damage that occurs during a stroke or other cerebral ischemic event. The present compounds can be used to treat a patient that has suffered a significant decrease in blood flow (creating localized low oxygen levels -- i.e. localized hypoxic conditions) followed by reperfusion of the tissues. To clarify the scope of claim 9, applicants have amended the claims to state that the method is directed to preventing or limiting tissue damage that results from an ischemic event. This amendment is not believed to reduce the scope of the claim, but merely to clarify the type of tissue damage the compounds can protect against.

Applicants respectfully submit that one of ordinary skill in the art would readily appreciate whether or not their actions fall within the scope of the amended claims. Therefore applicant respectfully submit they have fully complied with the requirements of 35 USC § 112, second paragraph and request the withdrawal of the rejections under that statutory section.

Claims 4-17 stand rejected under 35 USC § 112, first paragraph for lack of an enabling description. Applicants respectfully traverse and note that the invention is an improvement of an existing FDA approved compound that has been extensively studied. Felbamate (2-phenyl-1,3-propanediol dicarbamate) was FDA approved in July 1993 for the treatment of several forms of epilepsy. Additional investigations have reveal that this compound has activity in reducing cellular damage resulting from an ischemic event and subsequent vascular reperfusion (see US Patent Nos. 5,462,966 and 5,055,489). However, within the first year of felbamate's wide spread use, adverse reactions were reported, notably aplastic anemia and hepatotoxicity. The present invention is directed to a modified form of felbamate that prevents the formation of the toxic metabolites responsible for the reported adverse reactions.

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In addition to blocking the formation of the proposed toxic metabolite, the present derivatives have also been found to exhibit a similar activity profile relative to the parent compound. The felbamate derivatives of the captioned application were submitted to the National Institute of Neurological Disorders and Stroke (NINDS) for evaluation in a standard panel of assays. Two convulsant tests (MES and scMET), and a toxicity screen (rotorod in mice, positional sense and gait in rats) were employed for evaluating the compounds activity as neuroprotecting agents (see Example 3 of the application). The results of these tests revealed that the activity of the felbamate derivatives correlates well with the activity of the felbamate parent compound. Based on these results, applicants respectfully submit there is no reason not to expect the modified compounds to display the full range of activities that have already been reported for the parent felbamate compound.

The Examiner has cited a lack of predictability in the field as well as the broad range of disease states treatable by the claimed method as reasons why the present invention is not enabled. Applicants respectfully submit that in light of applicants' NINDS data, issues relating to predictability have been addressed. Furthermore, since the modifications necessary to preclude the formation of the toxic metabolites do not appear to effect the activity associated with the parent compound, there is no reason to doubt applicants' assertion that the modified compounds will exhibit the full range of activities that have been previously demonstrated for the parent compound.

The improvement of the present invention relates to a modification of the parent compound that prevents the formation of toxic metabolites. As shown in Examples 3 and 4 the modified compounds exhibit similar properties (i.e. function as a neuroprotective agent with a similar low toxicity) as the parent compound. The parent compound has been extensively tested and found to have activity in many other biomedical applications. Applicants have simply availed themselves of the detailed prior art teachings with regards to the uses of the parent felbamate compound and applied them to the new derivative compounds. In light of applicants' data described in Examples 3 and 4, there is simply no reason to doubt the objective teachings of the

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present application. Applicants respectfully submit the claimed invention fully complies with the requirements of 35 USC § 112, first paragraph and applicants request the withdrawal of the rejection under that statutory section.

The application as amended is believed to be in condition for allowance and applicants hereby request the withdrawal of the rejection under 35 USC § 112, second paragraph and 35 USC § 112, first paragraph and passage of the application to issuance. The Commissioner is hereby authorized to charge any fees due for this submission to Deposit Account No. 50-0423, as well as credit any refunds.

Respectfully submitted,

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